UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/764,818	01/26/2004	Patricia A. Brown	108328.00170 (AVSI-0033)	8276

25555 7590 12/11/2006

JACKSON WALKER LLP
901 MAIN STREET
SUITE 6000
DALLAS, TX 75202-3797

EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 12/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/764,818	BROWN.ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 7-9, 11, 15-20, 22, 23, 26-28, 30, 34-45, 47, 48, and 52-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-4,7-9,11-20,22,23,26-28,30-45,47-57,63,69,75,77,79,80,86,89,97 and 99.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 12-14,31-33,49-51,63,69,75,77,79,80,86,89,97 and 99.

DETAILED ACTION

An amendment was received and entered on 11/6/06.

Claims 5, 6, 24, 25, 46, 58-62, 64-68, 70-74, 76, 82-85, and 88 were canceled.

Claims 1-4, 7-9, 11-20, 22, 23, 26-28, 30-45, 47-57, 63, 69, 75, 77, 79, 80, 86, 89, 97, and 99 remain pending in the instant application.

Claims 12-14, 31-33, 49-51, 63, 69, 75, 77, 79, 80, 86, 89, 97, and 99 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/15/06.

Claims 1-4, 7-9, 11, 15-20, 22, 23, 26-28, 30, 34-45, 47, 48, and 52-57 are under consideration in this Office Action.

Rejections Withdrawn

Rejections not reiterated from the previous action are withdrawn.

Claim Objections

Claims 1, 23, and 44 are objected to as ungrammatical. Each instance of "identical" should be replaced by "identity".

Removal of the parentheses around "SEQ ID NO.: 1" is suggested in claims 1, 20, 23, 39, 44, 57

Insertion of a space in claims 30, 48, and 86 between 'Q' and 'I' of "SEQID" is suggested.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 1-4, 7-9, 11, 15-20, 22, 23, 26-28, 30, 34-45, 47, 48, and 52-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims have been amended to recite "95% identical to (SEQ ID NO:1)". The specification as filed provides no written support for this limitation, and Applicant has pointed to no support in the specification. At page 27 of the response, Applicant asserts that the Examiner has indicated that the specification supports such an amendment. This is not the case, the Examiner has never indicated that the specification supports the specific limitation "95% identical to (SEQ ID NO:1)".

Written Description

Claims 1-4, 7-9, 11, 15-20, 22, 23, 26-28, 30, 34-45, 47, 48, and 52-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written

description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4, 7-9, 11, 15-20, 22, 23, 26-28, 30, 34-45, 47, 48, and 52-57 are drawn to the genus of synthetic muscle-specific promoters. The specification discloses two examples of this genus (see e.g. Table 2 at page 40). It is apparent to one of skill in the art that there is a wide variety of proteins that are specific to muscles, e.g. troponins C, I, and T, dystrophin, myosin, beta actin, muscle creatine kinase, etc. However, the specification does not disclose the structures that are required to confer muscle-specific activity of the promoters governing expression of these genes. Therefore, although only two species are disclosed, the specification fails to identify relevant identifying characteristics, such as a correlation between structure and function, that are required for the claimed function. As a result, one of skill in the art could not conclude that Applicant was in possession of the claimed genus at the time the application was filed.

Response to Arguments

Applicant's arguments filed 11/6/06 have been fully considered but they are not persuasive.

At pages 28 and 29 of the response Applicant argues that one of skill in the art understands that the genus of synthetic promoters capable of driving expression of GHRH in muscle tissue is "within the spirit and scope of the claims." Applicant also

argues that promoters so structurally mutated from the two disclosed examples are not within the scope of the claims. For support Applicant relies on the specification which teaches two species of the genus, cites references for identifying and assaying tissue specific promoters, and directs one of skill in the art to obtain them from databases such as GenBank or the NCBI PubMed site. Applicant also relies on the findings of the court in In re Dileone where it was found that in some situations a disclosure of compound A may enable one of skill to make compounds B and C, even if B and C have not been described.

Applicants arguments are unpersuasive. It is immaterial whether or not one of skill would understand that the genus of synthetic promoters capable of driving expression of GHRH in muscle tissue is within the spirit and scope of the claims. What matters is whether or not the genus was adequately described. Similarly, it is immaterial that non-functional promoters are excluded by the language of the claims. As discussed in the rejection and below, the issue is whether or not a representative number of functional promoters has been disclosed. It has not. Also, while it is true that in some cases description of 'A' provides enablement and written description for 'B' and 'C', it is equally true that in some cases it does not. This is determined on a case by case basis by applying the statutes and the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov).

The written description requirement for genus claims can be satisfied by disclosure of a representative number of species of the claimed genus. Disclosure can be by reduction to practice, complete structural description, or disclosure of relevant

identifying characteristics such as a correlation between structure and function common to the species of the genus. The specification has disclosed two species. However, there is a wide variety of genes comprising muscle specific promoter elements, such that the disclosure of two species would not convey to one of skill in the art that Applicant was in possession of the claimed genus. Further, the specification fails to identify relevant identifying characteristics, such as a correlation between structure and function, that are required for the claimed function. As a result, one of skill in the art could not conclude that Applicant was in possession of the claimed genus at the time the application was filed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 7-9, 11, 18-20, 22, 23, 26-28, 30, 37-39, 40-45, 47, 48, and 55-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al (WO 200261037 A2) in view of Aihara et al (Nature Biotech. 16: 867-870, 1998) and Simon (US 6,928,318).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome

by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Schwartz taught injection of pSPc5-12-HV-GHRH (SEQ ID NO:11) into the muscle of a farm animal, and subsequent electroporation at the site by the method of Aihara. Pigs are exemplified at the paragraph bridging pages 37 and 38. Other animals include dairy cows, see paragraph 23. Aihara taught a method of electroporating nucleic acids into muscle by inserting electrode needles into muscle such that they encompassed the site into which DNA is injected. See page 867, column 2, second full paragraph. So, it is clear that the method of Schwartz includes delivery of nucleic acid to an area of tissue that is surrounded by and penetrated with a plurality of needles.

Schwartz did not teach application of a constant current electrical pulse.

Simon taught an electroporation system for introducing nucleic acids into muscle that utilizes a constant-current pulse generator where the delivered current is constant

and substantially independent of a change in a resistance in the selected tissue. See specifically column 12 lines 17-51, and column 18, lines 55-58. Dev et al (US Patent 5,993,434).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the electroporation of Simon because it allows such advantages as enabling accurate measurement and recording of the entire time course of relevant electrical parameters during electroporation. This facilitates optimization of conditions. See column 18, lines 14-22.

Although the cited references are silent with respect to an involuntary cull and body condition score, the combined references render obvious all of the claimed active method steps, so the functional effects of the methods are considered to be inherent. With regard to limitations requiring a reduction in mortality of newborns (claims 3 and 4) note that Schwartz envisioned methods of delivery to pregnant farm animals. See paragraphs 15-22 at pages 6-12.

Regarding limitations concerning the mass of nucleic acid construct given, these limitations are obvious because the mass given is a result effective variable. See paragraph 140 on page 40 of Schwarz.

Claims 15-17, 34-36, and 52-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al (WO 200261037 A2), Aihara et al (Nature Biotech. 16: 867-870, 1998) and Simon (US 6,928,318), as applied to claims 1-4, 7-9, 11, 18-20, 23,

26-28, 30, 37-39, 40-45, 47, 48, and 55-57 above, and further in view of Fewell et al (US 2003/0109478).

The teachings of Schwartz, Aihara, and Simon are discussed above and render obvious methods of delivering to a farm animal SEQ ID NO:11 by injection into muscle and subsequent electroporation by positioning multiple needle electrodes around the injections site and delivering a constant current pulse.

These references do not teach use of a transfection-facilitating polypeptide.

Fewell taught a method of improving delivery of a nucleic acid expression construct to muscle cells in vivo comprising introducing into the muscle a nucleic acid expression construct and poly-L-glutamate, and electroporating the muscle tissue using needle electrodes. See entire document, e.g. first sentence of paragraph 109 at page 11, paragraphs 113 and 114, paragraph 123 bridging pages 12 and 13, paragraph 128 at page 13, and claim 79.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the poly-L-glutamate of Fewell in the method of Schwartz as modified above in order to obtain the reasonably expected improvement in delivery and expression.

Response to Arguments

Applicant's arguments filed 11/6/06 have been fully considered but they are not persuasive.

Applicant's arguments throughout the response that the references do not teach constant current electroporation are moot in view of the new grounds of rejection reciting the Simon reference which renders obvious methods of constant current electroporation.

At pages 31 and 32, Applicant appears to argue that the inherency arguments presented above regarding the outcomes of the various claimed methods are invalid. Applicant's arguments are unpersuasive. If the outcome of a set of method steps must be inherent in the steps. If the prior art either anticipates or renders obvious claimed method steps, then the outcome is similarly obvious. Applicant has presented no evidence or logic to indicate that there is any matter of chance involved that would invalidate the inherency finding.

Applicant argues impermissible hindsight at pages 32 and 33. First Applicant argues that it is impermissible to ignore the fact that Aihara did not use the claimed vector. In other words Applicant argues that it is impermissible to separate the general electroporation technique of Aihara from the specific method, i.e. electroporation of a specific vector. This is unpersuasive because Schwartz specifically referred to Aihara in the context of the electroporation technique. See paragraph bridging pages 37 and 38. it is clear that Schwartz relied upon Aihara to teach an electroporation technique, so Applicant's arguments are unpersuasive. Applicant also argues that the Examiner ignores the fact that the weight of the treated animals of Schwartz increased. However, Applicant fails to make clear how this affects the rejection in any way. None of the claims excludes any increase in mass of the treated animals. Finally Applicant argues

that Schwartz did not make any selection of treating only female animals. This is unpersuasive because Applicant is arguing limitations that are not in the claims. Further, the Schwartz reference now relied upon does in fact disclose treatment of pregnant animals. See above.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 7-9, 11, 18-20, 22, 23, 26-28, 30, 37-39, 40-45, 47, 48, and 55-57 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-23 of U.S. Patent No. 6,423,693, in view of Schwartz et al (US Patent 6,551,996) and Simon (US 6,928,318).

Claims 21-23 of '693 are drawn to methods of delivering to muscle cells in vivo an expression vector encoding GHRH, wherein the vector comprises 5' and 3' UTRs. The portion of the specification supporting the claims indicates that method is intended for livestock improvement. See column 3, lines 8 and 9, and column 35, lines 20-41.

The '693 patent does not claim a synthetic muscle specific promoter or constant current electroporation.

The '996 patent taught a method of injecting into muscle of a farm animal a plasmid vector encoding SEQ ID NO:1 (HV-GHRH, an optimized protease resistant form of GHRH) under the control of a synthetic muscle specific promoter (SPc5-12). The site of injection was subsequently subjected to electroporation. See column 6, lines 15-24, column 22, lines 10-30. The method is intended to improve growth performance and increase the efficiency of the animal. See abstract, column 8, lines 24-60, and column 17, lines 31-34.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the promoter of '996 in the method of '693. One would have been motivated to do so because '996 taught that the SPc5-12 promoter greatly exceeds the transcriptional potencies of natural muscle specific promoters. See column 3, lines 45-50.

Simon taught an electroporation system for introducing nucleic acids into muscle that utilizes a constant-current pulse generator where the delivered current is constant and substantially independent of a change in a resistance in the selected tissue. See

specifically column 12 lines 17-51, and column 18, lines 55-58. Dev et al (US Patent 5,993,434).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the electroporation of Simon because it allows such advantages as enabling accurate measurement and recording of the entire time course of relevant electrical parameters during electroporation. This facilitates optimization of conditions. See column 18, lines 14-22.

Although the cited references are silent with respect to an involuntary cull and body condition score, the combined references render obvious all of the claimed active method steps, so the functional effects of the methods are considered to be inherent.

Claims 15-17, 34-36, and 52-54 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-23 of U.S. Patent No. 6,423,693, Schwartz et al (US Patent 6,551,996), and Simon (US 6,928,318) as applied to claims 1-4, 7-9, 11, 18-20, 22, 23, 26-28, 30, 37-39, 40-45, 47, 48, and 55-57 above, and further in view of Fewell et al (US 2003/0109478).

The teachings of the '693 and '96 patents are discussed above. These references did not teach a transfection facilitating polypeptide.

Fewell taught a method of improving delivery of a nucleic acid expression construct to muscle cells in vivo comprising introducing into the muscle a nucleic acid expression construct and poly-L-glutamate, and electroporating the muscle tissue using needle electrodes. See entire document, e.g. first sentence of paragraph 109 at page

11, paragraphs 113 and 114, paragraph 123 bridging pages 12 and 13, paragraph 128 at page 13, and claim 79.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the poly-L-glutamate of Fewell in the method of '693 in order to obtain the reasonably expected improvement in delivery and expression.

Although the cited references are silent with respect to an involuntary cull and body condition score, the combined references render obvious all of the claimed active method steps, so the functional effects of the methods are considered to be inherent.

Response to Arguments

Applicant's arguments filed 11/6/06 have been fully considered but they are not persuasive.

Applicant's arguments throughout the response that the references do not teach constant current electroporation are moot in view of the new grounds of rejection reciting the Simon reference which renders obvious methods of constant current electroporation.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, J. Douglas Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Richard Schnizer, Ph.D.
Primary Examiner
Art Unit 1635